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SEARCH REQUEST FORM

Scientific and Technical Inf rmati n Center

Requester's Full Name: Josephine YOUNG Examiner #: 79813 Date: 10-16-02
Art Unit: 1623 Phone Number ~~30~~ 605-1201 Serial Number: 09/719,909
Mail Box and Bldg/Room Location: CM1 8E13 Results Format Preferred (circle): PAPER DISK (E-MAIL)

If more than one search is submitted, please prioritize searches in order of need. me)

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Inositolphosphoglycan and ribose for treatment of ischaemia-reperfusion injury

Inventors (please provide full names): RADEMACHER, Thomas William; GREENBAUM, Leslie; McLEAN, PATRICIA

Earliest Priority Filing Date: 06-29-1998

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.** Attached: 1) current claim set 2) assignment info

Please search:

(1) compositions comprising IPG, such as IPG type P, + ribose

(2) compositions comprising IPG, such as IPG type P, + ribose + (adenosine, Purine, nucleotide precursor)

(3) method to treat ischaemic-reperfusion injury using IPG, such as IPG type P, ONLY

(4) claim 14 - method to treat ischaemic-reperfusion injury

(5) method for preserving organ for transplantation using IPG, such as IPG type P, + ribose

(6) method to reduce loss of ATP using IPG, such as IPG type P, ONLY

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STAFF USE ONLY	**Type of Search**		**Vendors and cost where applicable**	
Searcher: D. Schreiber	NA Sequence (#)		STN	102.26
Searcher Phone #: 308-4292	AA Sequence (#)		Dialog	
Searcher Location: CM1 6A03	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 11/4/02	Bibliographic	✓	Dr.Link	
Date Completed: 11/5/02	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 31	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 42	Other		Other (specify)	

PTO-1590 (8-01)

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=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:00:37 ON 05 NOV 2002)
L40          41 DUP REM L39 (44 DUPLICATES REMOVED)

=> d que 140
L1          665 SEA RADEMACHER T?/AU
L2          685 SEA GREENBAUM L?/AU
L3         1227 SEA MCLEAN P?/AU
L5          122 SEA INOSITOLPHOSPHOGLYCAN#
L6          279 SEA INOSITOL(3A) PHOSPHOGLYCAN#
L7            1 SEA INOSITOL(3A) PHOSPHO(3A) GLYCAN#
L8        97128 SEA TYPE(3A) P
L9        61737 SEA RIBOSE#
L10      475840 SEA ADENOSINE#
L18       81240 SEA (ISCHAEM? OR ISCHEM?)(5A) REPERFUS?
L21        2692 SEA IPG?
L22         112 SEA L21 AND GLYCAN?
L23         299 SEA L21 AND INOSITOL?
L25         468 SEA L5 OR L6 OR L7 OR L22 OR L23
L26          31 SEA L21 AND L8
L27         469 SEA L25 OR L26
L28          20 SEA L27 AND ((L9 OR L10 OR L11 OR L12) OR (L14 OR L15 OR L16
                OR L17))
L29          62 SEA ((L1 OR L2 OR L3)) AND L27
L30           1 SEA L27 AND L18
L39          85 SEA (L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35) OR
                L37 OR L38
L40          41 DUP REM L39 (44 DUPLICATES REMOVED)


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L40  ANSWER 1 OF 41  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:10305  HCAPLUS
DOCUMENT NUMBER:          136:64163
TITLE:                    Materials and methods relating for the treatment and
                          diagnosis of pre-eclampsia
INVENTOR(S):              Schofield, Julian; Rademacher, Thomas William
PATENT ASSIGNEE(S):       University College London, UK
SOURCE:                   PCT Int. Appl., 45 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ----------------    ----  --------      ---------------  --------
     WO 2002000254       A2    20020103      WO 2001-GB2800   20010625
     WO 2002000254       A3    20020530
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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Search completed by David Schreiber 308-4292

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001074330 A5 20020108 AU 2001-74330 20010625

PRIORITY APPLN. INFO.: GB 2000-15625 A 20000626
WO 2001-GB2800 W 20010625

AB The present invention relates to use of GPI-PLD (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial GPI-PLD activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated GPI-PLD activity present in the placenta in pre-eclampsia may be correctable by administration of GPI-PLD to the mother to correct the problems caused by abnormal or dysregulated GPI-PLD, e.g. to reduce the abnormal release and in situ prodn. of placental **IPGs** (**inositol phosphoglycans**) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous GPI-PLD or a fragment thereof, e.g. an inactive GPI-PLD capable of competing with or displacing the abnormal or dysregulated GPI-PLD, e.g. from Apo-A1.

L40 ANSWER 2 OF 41 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2002:245321 SCISEARCH
THE GENUINE ARTICLE: 530JV
TITLE: Insulin reduces serum glycosylphosphatidylinositol phospholipase D levels in human type I diabetic patients and streptozotocin diabetic rats
AUTHOR: Schofield J N (Reprint); Stephens J W; Hurel S J; Bell K M; deSouza J B; **Rademacher T W**
CORPORATE SOURCE: Univ Coll London, Royal Free & Univ Coll Med Sch, Mol Med Unit, Dept Immunol & Mol Pathol, Windeyer Inst Med Sci, 46 Cleveland St, , London W1T 4JF, England (Reprint); Univ Coll London, Royal Free & Univ Coll Med Sch, Mol Med Unit, Dept Immunol & Mol Pathol, Windeyer Inst Med Sci, London W1T 4JF, England; Middlesex Hosp, Dept Endocrinol & Diabet, London, England; Rodaris Pharmaceut, Oxford, England
COUNTRY OF AUTHOR: England
SOURCE: MOLECULAR GENETICS AND METABOLISM, (FEB 2002) Vol. 75, No. 2, pp. 154-161.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 1096-7192.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The enzyme glycosylphosphatidylinositol phospholipase D has a postulated role in the insulin-mimetic signaling pathway of glycosylphosphatidylinositol compounds. We have investigated enzyme activity in the serum of human type I diabetic patients and plasma and tissues of streptozotocin-induced diabetic rats following insulin administration. In the human diabetic patients serum enzyme activity fell by an average of 10.6%, (SEM = 2.7; P = 0.008; n = 20) following administration of insulin. In addition serum enzyme activity appeared to be depleted by 27% (SEM = 8.8; P = 0.011; n = 10) compared to nondiabetic controls. In untreated diabetic rats plasma enzyme activity gradually increased 0.3-fold over a 6-week period ($P < 0.001$; n = 8), this increase was reversed and activity normalized when these animals were treated with insulin. Cloning of the rat glycosylphosphatidylinositol phospholipase D

cDNA enabled confirmation of the liver as the principal organ of synthesis. Analysis of mRNA levels in the livers of the diabetic rats showed that gene expression was reduced in the insulin-treated animals compared to the noninsulin-treated controls by 0.7-fold (P = 0.004; n = 4). Tissue enzyme activity was also reduced in the insulin-treated rats; in skeletal muscle enzyme activity was 0.3-fold lower (P = 0.001; n = 4). Insulin therefore decreases glycosylphosphatidylinositol phospholipase D synthesis in diabetic animals resulting in decreased serum enzyme levels, suggesting a relationship between this enzyme and the function of insulin. (C) 2002 Elsevier Science (USA).

L40 ANSWER 3 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:331859 BIOSIS
DOCUMENT NUMBER: PREV200200331859
TITLE: V3a induces mitogenesis in Vero cells and chick embryo fibroblasts.
AUTHOR(S): Korves, T. (1); Bradshaw, A.; Albracht, D.; Wanda, P.; Galasko, G.
CORPORATE SOURCE: (1) Southern Illinois University, Edwardsville, IL, 62025 USA
SOURCE: Transactions of the Illinois State Academy of Science, (2002) Vol. 95, No. Supplement, pp. 85. print.
Meeting Info.: 94th Annual Meeting of the Illinois State Academy of Science Edwardsville, Illinois, USA April 19-20, 2002
ISSN: 0019-2252.
DOCUMENT TYPE: Conference
LANGUAGE: English

L40 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833641 HCAPLUS
DOCUMENT NUMBER: 135:354965
TITLE: Gelatin in assays, kits and lateral flow devices for determining **inositol phosphoglycans** and diagnosing pre-eclampsia
INVENTOR(S): Williams, Philip; Bord, Stephanie; **Rademacher, Thomas William**
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001086292	A2	20011115	WO 2001-GB2082	20010511
WO 2001086292	A3	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-11590 A 20000512

Search completed by David Schreiber 308-4292

GB 2001-2566 A 20010201

AB Assays, kits and methods for detg. the presence or amt. **inositol phosphoglycans** (**IPG**) analytes in samples are disclosed based on the finding that **IPG** antigens are capable of binding to gelatin. These assays can be used in the diagnosis of conditions where the presence or amt. of these analytes is a diagnostic marker for a condition. Methods for the diagnosis of pre-eclampsia, distinguishing different type of pre-eclampsia, are disclosed and also methods for detg. the onset of labor in a patient. An ELISA assay was developed using gelatin as the capture agent and rabbit polyclonal anti-**IPG** sera and a goat anti-rabbit horseradish peroxidase conjugated antibody as a two-component developing agent to analyze pre-eclamptic urine samples.

L40 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833334 HCAPLUS
DOCUMENT NUMBER: 135:358109
TITLE: Preparation of **inositol phosphoglycan** derivatives as antidiabetics and **IPG** antagonists
INVENTOR(S): Martin-Lomas, Manuel; **Rademacher, Thomas William**; Caro, Hugo Noberto; Francois, Irene
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085747	A1	20011115	WO 2001-GB2093	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053767	A1	20011220	US 2001-798125	20010302

PRIORITY APPLN. INFO.:
GB 2000-11591 A 20000512
US 2000-203607P P 20000512
US 2001-798125 A 20010302

AB Compds. X-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an **inositolphosphoglycan** (**IPG**), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an **IPG** second messenger or an **IPG** antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic **IPG**-P and/or **IPG**-A activities mentioned above to det. whether they will be suitable for use a **IPG** mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can

also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, O-(2-amino-2-deoxy-D-glucopyranosyl)-.beta.(1,6)-D-3-O-methyl-chiro-**inositol** was prepd. and used to treat a condition ameliorated by administration of and **IPG** second messenger or an **IPG** antagonist.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833333 HCAPLUS
DOCUMENT NUMBER: 135:344674
TITLE: Preparation of **inositol** **phosphoglycan** derivatives as antidiabetics and **IPG** antagonists
INVENTOR(S): Martin-Lomas, Manuel; **Rademacher, Thomas William**; Caro, Hugo Noberto; Francois, Irene
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085746	A1	20011115	WO 2001-GB2083	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001056072	A1	20011227	US 2001-798124	20010302

PRIORITY APPLN. INFO.:
GB 2000-11592 A 20000512
US 2000-203599P P 20000512
US 2001-798124 A 20010302

AB Compds. X-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an **inositolphosphoglycan** (**IPG**), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an **IPG** second messenger or an **IPG** antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic **IPG**-P and/or **IPG**-A activities mentioned above to det. whether they will be suitable for use a **IPG** mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, 1'-D-6-O-(2'-amino-4'-O-phosphate-2'-deoxy-.alpha.-D-glucopyranosyl)-myo-**inositol**-1,2-cyclic phosphate was prepd. and used to treat a

condition ameliorated by administration of and **IPG** second messenger or an **IPG** antagonist.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833332 HCAPLUS
DOCUMENT NUMBER: 135:358108
TITLE: Preparation of **inositol phosphoglycans** as antidiabetics and **IPG** antagonists
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo Norberto; Francois, Irene; Martin-Lomas, Manuel
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085745	A1	20011115	WO 2001-GB2098	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001041677	A1	20011115	US 2001-798004	20010302

PRIORITY APPLN. INFO.:
GB 2000-11593 A 20000512
US 2000-203598P P 20000512
US 2001-798004 A 20010302

AB Compds. having a mimetic or antagonistic property of an **inositol phosphoglycan** Y-X-cyclitols wherein X and Y are sugar residue, cyclitol is substituted with phosphate, thiophosphate, phosphate ester, phosphonate, thiophosphate ester, thiophosphonate, phosphoramidite, phosphoramidate, cyclic phosphate, sulfur group, substituted hydroxyl group, halogen, and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an **IPG** second messenger or an **IPG** antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular, the compds. are based on the linkage of two or more sugar residues to a cyclitol. Effect of these compds. on the activity of PDH phosphatase, PDH kinase, and acetyl CoA carboxylase I is reported. Thus, O-.alpha.-D-galactopyranosyl-(1-4)-(2-amino-2-deoxy-.alpha.-D-glucopyranosyl)-(1-6)-D-myo-**inositol** was prepd. and tested as antidiabetics and **IPG** antagonist.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833327 HCAPLUS
DOCUMENT NUMBER: 135:358107
TITLE: Preparation of **inositol** phosphates to treat

a condition ameliorated by administration of and **IPG** second messenger or an **IPG** antagonist

INVENTOR(S): Martin-Lomas, Manuel; **Rademacher, Thomas William**; Caro, Hugo Norbert; Francois, Irene

PATENT ASSIGNEE(S): Rademacher Group Limited, UK

SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085740	A2	20011115	WO 2001-GB2088	20010511
WO 2001085740	A3	20020328		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001051606	A1	20011213	US 2001-798005	20010302
AU 2001060426	A5	20011120	AU 2001-60426	20010511

PRIORITY APPLN. INFO.:

GB 2000-11594	A	20000512
US 2000-203596P	P	20000512
US 2001-798005	A	20010302
US 2000-203599P	P	20000512
WO 2001-GB2088	W	20010511

AB Compds. X-1,6-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an **inositolphosphoglycan** (**IPG**), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an **IPG** second messenger or an **IPG** antagonist thereof. In particular, the compds. are based on the 1,6 linkage of a sugar residue and a cyclitol. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic **IPG**-P and/or **IPG**-A activities mentioned above to det. whether they will be suitable for use a **IPG** mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, 1'-D-6-O-(2'-amino-4'-O-phosphate-2'-deoxy-.alpha.-D-glucopyranosyl)-myo-**inositol**-1,2-cyclic phosphate was prepd. and used to treat a condition ameliorated by administration of and **IPG** second messenger or an **IPG** antagonist.

L40 ANSWER 9 OF 41 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2001412385 MEDLINE

DOCUMENT NUMBER: 21354778 PubMed ID: 11461192

TITLE: Reversal of type 2 diabetes in mice by products of malaria

Search completed by David Schreiber 308-4292

parasites. II. Role of **inositol phosphoglycans (IPGs)**.

AUTHOR: Elased K M; Gumaa K A; de Souza J B; Rahmoune H; Playfair J H; **Rademacher T W**

CORPORATE SOURCE: Rademacher Group Ltd, Arthur Stanley House, 6th Floor, 40-50 Tottenham Street, London W1P 9PG, United Kingdom.. Khalid.elased@rademacher.co.uk

SOURCE: MOLECULAR GENETICS AND METABOLISM, (2001 Jul) 73 (3) 248-58.
Journal code: 9805456. ISSN: 1096-7192.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004

AB We have previously shown that infection with Plasmodium yoelii malaria or injection of extracts from malaria-parasitized red cells induces hypoglycemia in normal mice and normalizes the hyperglycemia in mice made moderately diabetic with streptozotocin. **Inositol phosphoglycans (IPGs)** are released outside cells by hydrolysis of membrane-bound glycosylphosphatidylinositols (GPIs), and act as second messengers mediating insulin action. The C57BL/Ks-db/db and C57BL/6J-ob/ob mice offer good models for studies on human obesity and Type 2 diabetes. In the present study, we show that a single iv injection of **IPG**-A or **IPG**-P extracted from P. yoelii significantly ($P < 0.02$) lowers the blood glucose in STZ-diabetic, db/db, and in ob/ob mice for at least 4--6 h. Using rat white adipocytes, **IPG**-P increased lipogenesis by 20--30% in the presence and absence of maximal concentrations of insulin (10(-8) M) ($P < 0.01$) and stimulated pyruvate dehydrogenase (PDH) phosphatase in a dose-related manner. Both **IPG**-A and **IPG**-P inhibited c-AMP-dependent protein kinase (PKA) in a dose-related manner. Compositional analysis of **IPGs** after 24 h hydrolysis revealed the presence of myo-**inositol**, phosphorus, galactosamine, glucosamine, and glucose in both **IPG**-A and **IPG**-P. However, hydrolysis of **IPGs** for 4 h highlighted differences between **IPG**-A and **IPG**-P. There are some functional similarities between P. yoelii **IPGs** and those previously described for mammalian liver. However, this is the first report of the hypoglycemic effect of **IPGs** in murine models of Type 2 diabetes. We suggest that **IPGs** isolated from P. yoelii, when fully characterized, may provide structural information for the synthesis of new drugs for the management of diabetes mellitus.

L40 ANSWER 10 OF 41 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:782254 SCISEARCH
THE GENUINE ARTICLE: 467MA
TITLE: **Inositol phosphoglycans** and insulin sensitivity of adipocytes from two strains of rats; Relation to obesity.

AUTHOR: Kunjara S (Reprint); Greenbaum A L; **McLean P**; **Rademacher T W**

CORPORATE SOURCE: Univ Coll London, Sch Med, Dept Mol Pathol, London W1P 6DB, England
COUNTRY OF AUTHOR: England

SOURCE: DIABETOLOGIA, (AUG 2001) Vol. 44, Supp. [1], pp.

Search completed by David Schreiber 308-4292

A177-A177. MA 680.
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA.
ISSN: 0012-186X.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L40 ANSWER 11 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:911091 HCAPLUS
DOCUMENT NUMBER: 134:37032
TITLE: **Adenosine** diphosphatase and activators thereof and their therapeutic and diagnostic uses for preeclampsia and platelet aggregation-associated conditions
INVENTOR(S): **McLean, Patricia; Greenbaum, Leslie ; Rademacher, Thomas William**
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078330	A2	20001228	WO 2000-GB2333	20000616
WO 2000078330	A3	20010525		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1185295	A2	20020313	EP 2000-940550	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1999-14326 A 19990618
WO 2000-GB2333 W 20000616

AB Materials and methods are provided for the diagnosis and treatment of preeclampsia and related conditions characterized by platelet aggregation. **Adenosine** diphosphatase (ADPase) and activators of ADPase are used for the treatment of preeclampsia, in order to overcome the inhibition of ADPase by **inositol phosphoglycans** (**IPGs**). Also provided is a method for screening for compds. with ADPase-stimulatory activity in the presence or absence of **IPGs**.

L40 ANSWER 12 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:457304 HCAPLUS
DOCUMENT NUMBER: 133:55669
TITLE: Treatment and diagnosis of cancer using **inositolphosphoglycans** antagonists
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 48 pp.

Search completed by David Schreiber 308-4292

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039589	A1	20000706	WO 1999-GB4382	19991223
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141723	A1	20011010	EP 1999-962426	19991223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533475	T2	20021008	JP 2000-591437	19991223

PRIORITY APPLN. INFO.: GB 1998-28564 A 19981223
WO 1999-GB4382 W 19991223

AB **Inositolphosphoglycans** (**IPGs**), and in particular A-type substances comprising myo-**inositol**, are tumor autocrine factors (TAFs), that is factors which cause tumor cell proliferation. The use of A-type **IPG** antagonists for the treatment of cancer and a method for the diagnosis or prognosis of cancer based on the presence or amt. of **IPGs** in a sample from a patient is disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:15024 HCAPLUS
DOCUMENT NUMBER: 132:59168
TITLE: **Inositolphosphoglycan** and **ribose** for treatment of **ischemia-reperfusion** injury
INVENTOR(S): **Rademacher, Thomas William; Greenbaum, Leslie; McLean, Patricia**
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000205	A1	20000106	WO 1999-GB1499	19990512
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2332969	AA	20000106	CA 1999-2332969	19990512
AU 9939402	A1	20000117	AU 1999-39402	19990512
AU 748892	B2	20020613		
EP 1091743	A1	20010418	EP 1999-922293	19990512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002519328	T2	20020702	JP 2000-556790	19990512

PRIORITY APPLN. INFO.: GB 1998-14039 A 19980629
WO 1999-GB1499 W 19990512

AB Compns. comprising **inositolphosphoglycans** (**IPGs**) and **ribose** are disclosed, and their use in the prevention or treatment of **ischemic-reperfusion** injury. This treatment increases the energy generating systems of cells by employing the mitochondrial oxidative restoration system. The use of the compns. in preserving organs for **transplantation** is also disclosed.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 14 OF 41 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000513875 MEDLINE
DOCUMENT NUMBER: 20522979 PubMed ID: 11072827
TITLE: **Inositolphosphoglycan** mediators structurally related to glycosyl phosphatidylinositol anchors: synthesis, structure and biological activity.
AUTHOR: Martin-Lomas M; Khiar N; Garcia S; Koessler J L; Nieto P M; **Rademacher T W**
CORPORATE SOURCE: Grupo de Carbohidratos, Instituto de Investigaciones Quimicas CSIC-UNSE, Sevilla, Spain.. manuel.martin-lomas@iiq.cartuja.csic.es
SOURCE: CHEMISTRY, (2000 Oct 2) 6 (19) 3608-21.
Journal code: 9513783. ISSN: 0947-6539.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001128

AB The preparation of the pseudopentasaccharide 1a, an **inositol-phosphoglycan** (**IPG**) that contains the conserved linear structure of glycosyl phosphatidylinositol anchors (GPI anchors), was carried out by using a highly convergent 2+3-block synthesis approach which involves imidate and sulfoxide glycosylation reactions. The preferred solution conformation of this structure was determined by using NMR spectroscopy and molecular dynamics simulations prior to carrying out quantitative structure--activity relationship studies in connection with the insulin signalling process. The ability of 1a to stimulate lipogenesis in rat adipocytes as well as to inhibit cAMP dependent protein kinase and to activate pyruvate dehydrogenase phosphatase was investigated. Compound 1a did not show any significant activity, which may be taken as a strong indication that the GPI anchors are not the precursors of the **IPG** mediators.

L40 ANSWER 15 OF 41 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V. DUPLICATE 3
ACCESSION NUMBER: 2000379706 EMBASE
TITLE: Structure and expression of the human

glycosylphosphatidylinositol phospholipase D1 (GPLD1) gene.
AUTHOR: Schofield J.N.; **Rademacher T.W.**
CORPORATE SOURCE: J.N. Schofield, Molecular Medicine Unit, Department of Molecular Pathology, University College London, 46 Cleveland Street, London W1P 6DB, United Kingdom
SOURCE: Biochimica et Biophysica Acta - Gene Structure and Expression, (15 Nov 2000) 1494/1-2 (189-194).
Refs: 23
ISSN: 0167-4781 CODEN: BBGSD5
PUBLISHER IDENT.: S 0167-4781(00)00194-9
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Here we report the structure of the human glycosylphosphatidylinositol phospholipase D1 gene, which covers at least 80 kb on chromosome 6p22. The gene comprises 25 exons and encodes a 5.8 kb mRNA, which was detected only in the liver. Southern blot analysis shows that the human genome contains only one GPLD gene and we could only detect one of the two previously reported cDNAs. Copyright (C) 2000 Elsevier Science B.V.

L40 ANSWER 16 OF 41 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000188034 MEDLINE
DOCUMENT NUMBER: 20188034 PubMed ID: 10720442
TITLE: **Inositol phosphoglycans** and signal transduction systems in pregnancy in preeclampsia and diabetes: evidence for a significant regulatory role in preeclampsia at placental and systemic levels.
AUTHOR: Kunjara S; Greenbaum A L; Wang D Y; Caro H N; **McLean P**; Redman C W; **Rademacher T W**
CORPORATE SOURCE: Department of Molecular Pathology, Molecular Medicine Unit, The Windeyer Building, 46, University College London Medical School, Cleveland Street, London, W1P 6DB, England.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (2000 Feb) 69 (2) 144-58.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000606
Last Updated on STN: 20000606
Entered Medline: 20000519
AB Measurements have been made of the urinary content of **inositol phosphoglycans IPG P-type** and **IPG** A-type, putative insulin second messengers, in preeclampsia, in type I insulin-treated diabetic pregnant women and their matched control subjects, and nonpregnant women of child-bearing age. The content of **IPG P-type** and **IPG** A-type was also measured in the placenta from preeclamptic patients and from normal pregnancies. Pregnancy was associated with an increase, approximately twofold, in urinary output of **IPG-P-type** relative to nonpregnant controls ($P<0.01$). The 24-h output of **IPG P-type** in urine in preeclamptic women was significantly higher (2- to 3-fold) than in pregnant control subjects matched for age, parity, and stage of gestation ($P<0.02$). In contrast, insulin-dependent

diabetic pregnant women did not show any significant change in urinary output of **IPG P-type** or **IPG** A-type relative to pregnant control subjects. Evidence for a possible relationship and correlation between the urinary excretion of **IPG P-type** and markers of preeclampsia, including proteinuria ($r = 0.720$, $P<0.01$), plasma aspartate transaminase ($r = 0.658$, $P<0.05$), and platelet counts ($r = 0.613$, $P<0.05$) is presented. A high yield of **IPG P-type** was extracted from human placenta, in preeclampsia some 3-fold higher ($P = 0.03$) than the normal value, whereas no **IPG** A-type (with lipogenic-stimulating activity) was found. Low concentrations of placental **IPG** A-type were detected relative to **IPG P-type** using assay systems dependent upon the effect of this mediator on cAMP-dependent protein kinase or on a proliferation assay using thymidine incorporation into DNA of EGFR T17 fibroblasts. It is postulated that the high urinary excretion **IPG P-type** in preeclampsia reflects high placental levels and relates to the accumulation of glycogen in the placenta. The paracrine effects of placental **IPG P-type** (stimulation off other endocrine glands and/or endothelial cells) could contribute to the pathogenesis of the maternal syndrome. A possible theoretical link between elevated placental **IPG P-type** and **apoptosis** is proposed.

L40 ANSWER 17 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:50486 BIOSIS
DOCUMENT NUMBER: PREV200100050486
TITLE: **Inositol phosphoglycans (IPGS**) derived from Plasmodium yoelii mimic insulin action in vivo.
AUTHOR(S): Elased, K. M. (1); Gumaa, K. A. (1); de Souza, J. B.; **Rademacher, T. W.**
CORPORATE SOURCE: (1) Rademacher Group Ltd, 40-50 Tottenham Street, Arthur Stanley House, 6th Floor, London, W1P 9PG UK
SOURCE: Journal of Endocrinology, (November, 2000) Vol. 167, No. Supplement, pp. P62. print.
Meeting Info.: 191st Meeting of the Society for Endocrinology London, England, UK November 20-21, 2000 Society for Endocrinology
. ISSN: 0022-0795.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L40 ANSWER 18 OF 41 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000295348 MEDLINE
DOCUMENT NUMBER: 20295348 PubMed ID: 10833332
TITLE: **Inositol phosphoglycans** and the regulation of the secretion of leptin: in vitro effects on leptin release from adipocytes and the relationship to obesity.
AUTHOR: Kunjara S; Wang D Y; **McLean P**; Greenbaum A L; **Rademacher T W**
CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, UK.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (2000 May) 70 (1) 61-8. Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000719

AB The ratio of two families of **inositol phosphoglycans** (**IPG**-A:**IPG**-P), insulin second messengers, is raised in non-insulin-dependent diabetes mellitus (NIDDM) and obesity. It is shown here that **IPG** A type inhibits leptin release from adipocytes, contrasting with the action of insulin (stimulation) and **IPG P type** (no effect). The significance of inhibitory effects of **IPG** A type on leptin release is important in relation to obesity and NIDDM in view of the action of leptin in promoting Lep expression and fat oxidation in muscle, in addition to its effects on satiety. Energy conservation and oxidation via interorgan regulation by leptin could be compromised by a rise in the **IPG**-A:**IPG** -P ratio.

L40 ANSWER 19 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:640696 HCAPLUS
DOCUMENT NUMBER: 131:256346
TITLE: Antagonism of **inositolphosphoglycan** signaling in mast cells, basophils and eosinophils
INVENTOR(S): **Rademacher, Thomas William**; Whitby, Helen
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949855	A2	19991007	WO 1999-GB981	19990329
WO 9949855	A3	19991118		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319588	AA	19991007	CA 1999-2319588	19990329
AU 9931596	A1	19991018	AU 1999-31596	19990329
EP 1066043	A2	20010110	EP 1999-913481	19990329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-6645 A 19980327
WO 1999-GB981 W 19990329

AB The authors disclose that **inositolphosphoglycans** (**IPGs**) can be obtained from basophils, eosinophils and mast cells and that allergen stimulation of these cells results in **IPG** release. **IPGs**, acting as second messengers in non-allergen stimulated

cells, induced histamine release or degranulation. Thus, **IPG** antagonists are envisioned for the treatment of conditions (esp. allergy and asthma) mediated by the release of **IPGs** from mast cells, basophils or eosinophils. Preferred **IPG** antagonists include anti-**IPG** antibodies, inhibitors of the enzyme glycosylphosphatidylinositol phospholipase D, and competitive antagonists.

L40 ANSWER 20 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:614255 HCAPLUS
DOCUMENT NUMBER: 131:237961
TITLE: Materials and methods using antibody binding for identifying **inositolphosphoglycan** mimetics
INVENTOR(S): **Rademacher, Thomas William**; Williams, Phillip
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947926	A2	19990923	WO 1999-GB845	19990318
WO 9947926	A3	19991104		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321734	AA	19990923	CA 1999-2321734	19990318
AU 9929468	A1	19991011	AU 1999-29468	19990318
EP 1066521	A2	20010110	EP 1999-910536	19990318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002507724	T2	20020312	JP 2000-537070	19990318

PRIORITY APPLN. INFO.: GB 1998-5771 A 19980318
WO 1999-GB845 W 19990318

AB Methods for detg. a binding profile for an **inositolphosphoglycan** (**IPG**) or a candidate mimetic compd. are disclosed in which the **IPG** or candidate mimetic compd. is contacted with an anti-**IPG** antibody in a binding assay and the binding of the **IPG** or candidate mimetic compd. to the antibody is used to establish the binding profiles. The profiles are then used in methods for identifying candidate compds. for further testing or development as **IPG** mimetics, providing lead compds. for further development as pharmaceuticals.

L40 ANSWER 21 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:613973 HCAPLUS
DOCUMENT NUMBER: 131:241984
TITLE: Anti-**inositolphosphoglycan** monoclonal antibodies
INVENTOR(S): Nieto, Isabel Varela; Mato, Jose; Prieto, Jesus;

Williams, Phillip; **Rademacher, Thomas William**
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947565	A1	19990923	WO 1999-GB844	19990318
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321113	AA	19990923	CA 1999-2321113	19990318
AU 9929467	A1	19991011	AU 1999-29467	19990318
AU 748080	B2	20020530		
EP 1062246	A1	20001227	EP 1999-910535	19990318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002506631	T2	20020305	JP 2000-536756	19990318

PRIORITY APPLN. INFO.:
GB 1998-5739 A 19980318
GB 1998-11000 A 19980521
WO 1999-GB844 W 19990318

AB The present invention relates to anti-**IPG** antibodies, and in particular monoclonal antibodies produced by hybridoma cell lines 2F7, 2D1 and 5H6, and the use of these and other similar antibodies in the treatment and diagnosis of pre-eclampsia or diabetes, esp. type I diabetes. A method of producing anti-**IPG** antibodies by immunizing an animal with **IPG** unconjugated to an immunogenic carrier is also disclosed.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 22 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:495179 HCAPLUS
DOCUMENT NUMBER: 131:125475
TITLE: Neurotrophic properties of **IPGs** and **IPG** analogues
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo Norberto; Martin-Lomas, Manuel; Nieto, Isabel Varela; Alvarez, Yolanda Leon
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9938516 A1 19990805 WO 1998-GB3847 19981221
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2318584 AA 19990805 CA 1998-2318584 19981221
AU 9917708 A1 19990816 AU 1999-17708 19981221
EP 1064003 A1 20010103 EP 1998-962574 19981221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002501899 T2 20020122 JP 2000-529249 19981221
PRIORITY APPLN. INFO.: GB 1998-1899 A 19980129
WO 1998-GB3847 W 19981221

AB **Inositolphosphoglycans** (**IPGs**) or **inositol** -contg. **IPG** analogs can be used to specifically cause neuron proliferation or neuron differentiation, and in particular neurite outgrowth. **P-type IPGs** or chiro-**inositol** contg. analogs cause neurite outgrowth and A-type **IPGs** or myo-**inositol** contg. analogs cause neuron proliferation. Compns. comprising these agents and their medical uses are also disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 23 OF 41 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000076804 MEDLINE
DOCUMENT NUMBER: 20076804 PubMed ID: 10607479
TITLE: **Inositol phosphoglycans** in diabetes and obesity: urinary levels of **IPG** A-**type** and **IPG P-type**, and relationship to pathophysiological changes.
AUTHOR: Kunjara S; Wang D Y; Greenbaum A L; **McLean P**; Kurtz A; **Rademacher T W**
CORPORATE SOURCE: Department of Molecular Pathology, Molecular Medicine Unit, University College London Medical School, The Windeyer Building, 46, Cleveland Street, London, W1P 6DB, United Kingdom.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (1999 Dec) 68 (4) 488-502.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000301

AB Measurements have been made, in adult male diabetic patients and control subjects, of the urinary content of **inositol** **phosphoglycans** (**IPGs**), the **IPG** A-**type** and **IPG P-type** forms, which, among other actions, regulate pathways of glucose utilization, lipogenesis, triglyceride formation, and pyruvate dehydrogenase (PDH) activity. Urine

samples from the entire diabetic group showed a 2- to 3-fold increase in **IPG** A-type, and a fall in the **IPG P-type:IPG** A-**type** ratio relative to the control group. Subdivision of the diabetic patients into lean IDDM and obese NIDDM groups revealed significant differences in the **IPG P-type:IPG** A-**type** ratio between these groups, this ratio decreasing with increases in the body mass index (BMI). Analysis of the relationships among **IPGs** and HbA1, blood pressure, and BMI indicated that a fall in the **IPG P-type:IPG** A-**type** ratio correlated with a rise in the HbA1 (indicative of impaired glycemic control), with increased systolic blood pressure and increased obesity, all factors linked to Syndrome X. There was a parallism between the profile of the **IPG P-type:IPG** A-**type** ratio and the well-established pattern of insulin resistance and BMI. In vitro studies of the effects of alterations in the **IPG P-type:IPG** A-**type** ratio on the activation of the pyruvate dehydrogenase complex (PDH complex) at the PDH phosphatase reaction demonstrated that **IPG** A-type forms antagonized the stimulation of the PDH phosphatase by **IPG P-type** forms, thus having a negative effect on the conversion of PDH to the active, dephosphorylated, form. This observation could provide a mechanism whereby the shifts in the **IPG P-type :IPG** A-**type** ratio reported above could change the metabolic pattern from one directed to glucose oxidation to one more directed toward energy conservation and lipid storage.

L40 ANSWER 24 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:393699 BIOSIS
DOCUMENT NUMBER: PREV199900393699
TITLE: Higher detection of **inositolphosphoglycans** (**IPG**) in pre-eclamptic than in normal placenta by immunohistochemical staining.
AUTHOR(S): Deborde, S. (1); Sooranna, S. R.; Williams, P. J. (1); Mato, J.; **Rademacher, T. W. (1)**
CORPORATE SOURCE: (1) Molecular Medicine Unit, Department of Molecular Pathology, UCL, London UK
SOURCE: Placenta, (July-Aug., 1999) Vol. 20, No. 5-6, pp. A.21. Meeting Info.: 5th Conference of the International Federation of Placenta Associations and the 8th Meeting of the European Placenta Group Schladming, Austria September 26-29, 1999 European Placenta Group . ISSN: 0143-4004.
DOCUMENT TYPE: Conference
LANGUAGE: English

L40 ANSWER 25 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:393697 BIOSIS
DOCUMENT NUMBER: PREV199900393697
TITLE: Investigation of **inositolphosphoglycans** (**IPG**) activity in the brush border membrane of normal and pre-eclamptic (PE) human placenta.
AUTHOR(S): Deborde, S. (1); Kunjara, S. (1); **Rademacher, T. W. (1)**
CORPORATE SOURCE: (1) Mol Med Unit, Department of Molecular Pathology, UCL, London UK
SOURCE: Placenta, (July-Aug., 1999) Vol. 20, No. 5-6, pp. A.20. Meeting Info.: 5th Conference of the International

Federation of Placenta Associations and the 8th Meeting of the European Placenta Group Schladming, Austria September 26-29, 1999 European Placenta Group . ISSN: 0143-4004.
DOCUMENT TYPE: Conference
LANGUAGE: English

L40 ANSWER 26 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:184077 HCAPLUS
DOCUMENT NUMBER: 128:226252
TITLE: Materials and methods using **P**- and A-**type inositolphosphoglycans** and their antagonists for the diagnosis and treatment of diabetes and associated obesity
INVENTOR(S): **Rademacher, Thomas William; McLean, Patricia**
PATENT ASSIGNEE(S): Hoeft Rademacher Limited, UK; Rademacher, Thomas William; McLean, Patricia
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811435	A1	19980319	WO 1997-GB2440	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741304	A1	19980402	AU 1997-41304	19970911
AU 722425	B2	20000803		
EP 925503	A1	19990630	EP 1997-939083	19970911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1234118	A	19991103	CN 1997-199097	19970911
BR 9711753	A	20000118	BR 1997-11753	19970911
JP 2001505658	T2	20010424	JP 1998-513366	19970911

PRIORITY APPLN. INFO.: GB 1996-18934 A 19960911
WO 1997-GB2440 W 19970911

AB The diagnosis of diabetes based on the level or ratio of **P**- and A-**type inositolphosphoglycans** (**IPGs**) in a sample from a patient, and the use of **P**- and A-**type IPGs** or their antagonists in the treatment of diabetes, are disclosed. In particular, the invention provides treatment of IDDM or lean type II diabetes (NIDDM) with a mixt. of **P**- and A-**type** mediators, and treatment of obese type II diabetes (NIDDM) with a **P**-**type** mediator and/or an A-type antagonist.

L40 ANSWER 27 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180889 HCAPLUS
DOCUMENT NUMBER: 128:240997
TITLE: Cyclitol containing carbohydrates from human tissue

which regulate glycogen metabolism and their use in pharmaceuticals
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811117	A1	19980319	WO 1997-GB2533	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743101	A1	19980402	AU 1997-43101	19970911
AU 713100	B2	19991125		
EP 925304	A1	19990630	EP 1997-919168	19970911
EP 925304	B1	20000426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 192160	E	20000515	AT 1997-919168	19970911
ES 2147988	T3	20001001	ES 1997-919168	19970911
JP 2001500859	T2	20010123	JP 1998-513410	19970911
US 6271204	B1	20010807	US 1999-254748	19990614

PRIORITY APPLN. INFO.: GB 1996-18929 A 19960911
WO 1997-GB2533 W 19970911

AB The application relates to the purifn. and characterization of a family of **P-type inositolphosphoglycans** (**IPGs**) from human liver and placenta. These substances are shown to have **P-type** biol. activity, e.g., activating pyruvate dehydrogenase (PDH) phosphatase. The characterization of the compds. demonstrates that they contain metal ions, in particular Mn2+ and/or Zn2+, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g., for the treatment of diabetes, and in screening for synthetic analogs.

L40 ANSWER 28 OF 41 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180888 HCAPLUS
DOCUMENT NUMBER: 128:242350
TITLE: A type A glycosylphosphatidylinositol second messenger from human tissue involve in regulation of lipogenesis
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811116	A1	19980319	WO 1997-GB2444	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741307	A1	19980402	AU 1997-41307	19970911
AU 713103	B2	19991125		
EP 925305	A1	19990630	EP 1997-939087	19970911
EP 925305	B1	20000426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 192161	E	20000515	AT 1997-939087	19970911
ES 2147996	T3	20001001	ES 1997-939087	19970911
JP 2001504450	T2	20010403	JP 1998-513368	19970911
US 6303580	B1	20011016	US 1999-254797	19990604
US 2001039027	A1	20011108	US 2001-775856	20010201

PRIORITY APPLN. INFO.:		
GB 1996-18930	A	19960911
WO 1997-GB2444	W	19970911
US 1999-254797	A3	19990604

AB A family of A-type **inositolphosphoglycans** (**IPGs**) from human liver and placenta that appear to play a role in the regulation of lipogenesis are identified and characterized. These substances have the biol. activity assocd. with A-type **IPG** fractions, namely regulating lipogenic activity and inhibiting cAMP dependent protein kinase. The characterization of the compds. demonstrates that they contain metal ions, in particular Zn2+, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g. for the treatment of diabetes, and in screening for synthetic analogs.

L40 ANSWER 29 OF 41 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1998:180785 HCAPLUS
DOCUMENT NUMBER:	128:226268
TITLE:	**P-type inositolphosphoglycans** and antagonists thereof in diagnosis and treatment of pre-eclampsia and diabetes
INVENTOR(S):	**Rademacher, Thomas William; Mclean, Patricia**
PATENT ASSIGNEE(S):	Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Mclean, Patricia
SOURCE:	PCT Int. Appl., 63 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810791	A1	19980319	WO 1997-GB2534	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,				

KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

AU 9743102	A1	19980402	AU 1997-43102	19970911
AU 715884	B2	20000210		
EP 939651	A1	19990908	EP 1997-919169	19970911
EP 939651	B1	20000531		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

CN 1235556	A	19991117	CN 1997-199318	19970911
BR 9711752	A	20000118	BR 1997-11752	19970911
AT 193452	E	20000615	AT 1997-919169	19970911
ES 2148967	T3	20001016	ES 1997-919169	19970911
JP 2001501598	T2	20010206	JP 1998-513411	19970911

PRIORITY APPLN. INFO.: GB 1996-18931 A 19960911
WO 1997-GB2534 W 19970911

AB The invention relates to materials and methods for the diagnosis and treatment of pre-eclampsia, and more particularly to the role of **P-type inositolphosphoglycans** (**IPGs**) in the occurrence of pre-eclampsia. Methods of diagnosing pre-eclampsia by detg. the level of **P-type IPGs** and uses of antagonists of **P-type IPGs** in the treatment of pre-eclampsia are disclosed, together with a method for screening for **P-type IPG** antagonists.

L40 ANSWER 30 OF 41 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:400348 SCISEARCH
THE GENUINE ARTICLE: 197JY
TITLE: Glycosyl phosphatidylinositol (GPI)/**inositolphosphate glycan** (**IPG**): An intracellular signalling system involved in the control of thyroid cell proliferation
AUTHOR: Petitfrere E (Reprint); Sartelet H; Vivien D; VarelaNieto I; Elbtaouri H; Martiny L; Haye B
CORPORATE SOURCE: UFR SCI REIMS, BIOCHIM LAB, CNRS, UPRES A, BP 1039, F-51687 REIMS 2, FRANCE (Reprint); UNIV CAEN, NEUROSCI LAB, CNRS, URA 1829, F-14043 CAEN, FRANCE; CSIC, INST INVEST BIOMED, MADRID 28029, SPAIN
COUNTRY OF AUTHOR: FRANCE; SPAIN
SOURCE: BIOCHIMIE, (DEC 1998) Vol. 80, No. 12, pp. 1063-1067. Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER, 23 RUE LINOIS, 75724 PARIS CEDEX 15, FRANCE. ISSN: 0300-9084.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In porcine thyrocytes, TSH alone does not induce cell growth. Recently, it has been demonstrated that acute stimulation by TSH of porcine thyrocytes leads to release an **inositolphosphate glycan** (**IPG**) described as a putative second messenger for various growth factors in different cell types. **IPG** isolated from porcine thyrocytes induces proliferation of fibroblasts EGFR T17 and porcine thyrocytes. In porcine thyrocytes we have confirmed that cell growth requires the presence of both TSH and insulin. This effect is

reproduced by 8-bromo cyclic AMP suggesting a mediation by intracellular cyclic AMP. Cooperative effects between 8-bromo cyclic AMP and **IPG** have also been evidenced and are in favour of a crosstalk between distinct signalling pathways. (C) Societe francaise de biochimie et biologie moleculaire / Elsevier, Paris.

L40 ANSWER 31 OF 41 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1998399980 MEDLINE
DOCUMENT NUMBER: 98399980 PubMed ID: 9729619
TITLE: cGMP inhibits IP3-induced Ca2+ release in intact rat megakaryocytes via cGMP- and cAMP-dependent protein kinases.
AUTHOR: Tertyshnikova S; Yan X; Fein A
CORPORATE SOURCE: Department of Physiology, University of Connecticut Health Center, Farmington, CT, USA.
SOURCE: JOURNAL OF PHYSIOLOGY, (1998 Oct 1) 512 (Pt 1) 89-96. Journal code: 0266262. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981202

AB 1. Inhibition of **inositol** 1,4,5-trisphosphate (IP3) receptor-mediated Ca2+ release by cGMP was examined in intact rat megakaryocytes, by using a combination of single cell fluorescence microscopy to monitor intracellular free **calcium** ([Ca2+]i) and flash photolysis of caged second messengers. 2. Sodium nitroprusside (SNP), a nitric oxide (NO) donor, and the hydrolysis-resistant cGMP analogue 8-(4-chlorophenylthio)guanosine 3',5'-cyclic monophosphate (pCPT-cGMP) inhibited Ca2+ release induced by photolysis of caged IP3. Neither of them affected the rate of Ca2+ removal from the cytoplasm following photolysis of caged Ca2+. 3. Photolysis of the caged NO donor 3-morpholinosydnonimine (SIN-1) during agonist-induced [Ca2+]i oscillations inhibited Ca2+ release without affecting the rate of Ca2+ uptake and/or extrusion. 4. We conclude that the inhibition of IP3-induced Ca2+ release is the principal mechanism of NO-cGMP-dependent inhibition of [Ca2+]i mobilization. 5. **IPG**, a specific peptide inhibitor of cGMP-dependent protein kinase (cGMP-PK), blocked the inhibitory effect of pCPT-cGMP, indicating that the inhibition of IP3-induced Ca2+ release by pCPT-cGMP is mediated by cGMP-PK. However, the simultaneous application of both **IPG** and IP20, a specific peptide inhibitor of cAMP-dependent protein kinase (cAMP-PK), was required to block the inhibitory effect of SNP. These data strongly suggest that NO-cGMP-dependent inhibition of [Ca2+]i mobilization is mediated via the activation of both cGMP-PK and cAMP-PK.

L40 ANSWER 32 OF 41 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 97406564 MEDLINE
DOCUMENT NUMBER: 97406564 PubMed ID: 9259987
TITLE: Isolation and partial characterisation of insulin-mimetic **inositol phosphoglycans** from human liver.
AUTHOR: Caro H N; Kunjara S; **Rademacher T W**; Leon Y; Jones D R; Avila M A; Varela-Nieto I
CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, United Kingdom.
SOURCE: BIOCHEMICAL AND MOLECULAR MEDICINE, (1997 Aug) 61 (2)

Search completed by David Schreiber 308-4292

214-28.
Journal code: 9508702. ISSN: 1077-3150.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 20000303
Entered Medline: 19971023

AB Extracts of human liver were found to contain activities which copurified and coeluted with the two major subtypes of mediators (**type** A and **type P**) isolated from insulin-stimulated rat liver. The putative type A mediator from human liver inhibited cAMP-dependent protein kinase from bovine heart, decreased phosphoenolypyruvate carboxykinase mRNA levels in rat hepatoma cells, and stimulated lipogenesis in rat adipocytes. The putative **type P** mediator stimulated bovine heart pyruvate dehydrogenase phosphatase. Both fractions were able to stimulate proliferation of EGFR T17 fibroblasts and the type A was able to support growth in organotypic cultures of chicken embryo cochleovestibular ganglia. Both activities were resistant to Pronase treatment and the presence of carbohydrates, phosphate, and free-amino groups were confirmed in the two fractions. These properties are consistent with the structure/ function characteristics of the **type** A and **P inositolphosphoglycans** (**IPG**) previously characterized from rat liver. Further, the ability of the human-derived mediators to interact with rat adipocytes and bovine-derived metabolic enzymes suggests similarity in structure between the mediators purified from different species. Galactose oxidase-susceptible membrane-associated glycosylphosphatidylinositols (GPI) have been proposed to be the precursors of **IPG**. GPI was purified from human liver membranes followed by treatment with galactose oxidase and reduction with NaB3H4. Serial t.l.c. revealed three radiolabeled bands which comigrated with the putative GPI precursors found in rat liver. These galactose-oxidase-reactive lipidic compounds, however, were only partially susceptible to hydrolysis with phosphatidylinositol-specific phospholipase C from Bacillus thuringiensis and were resistant to glycosylphosphatidylinositol-specific phospholipase C from Trypanosoma brucei. These data indicate that **IPG** molecules with insulin-like biological activities are present in human liver.

L40 ANSWER 33 OF 41 MEDLINE DUPLICATE 9

ACCESSION NUMBER: 97227170 MEDLINE
DOCUMENT NUMBER: 97227170 PubMed ID: 9132295
TITLE: **Inositol-phosphoglycan** inhibits **calcium** oscillations in hepatocytes by reducing **calcium** entry.
AUTHOR: Sanchez-Bueno A; Greenwood M R; Varela-Nieto I; Marrero I; Gil B; Mato J M; Cobbold P H
CORPORATE SOURCE: Department of Human Anatomy and Cell Biology, University of Liverpool, UK.. antonio@liverpool.ac.uk
SOURCE: CELL CALCIUM, (1997 Feb) 21 (2) 125-33.
Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704

ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507
Entered Medline: 19970430

AB **Inositol-phosphoglycan** (**IPG**) is a putative mediator of insulin action that has been shown to affect numerous biochemical processes. **IPG**, prepared from liver membranes, promptly inhibited phenylephrine- or vasopressin-induced [Ca2+]i oscillations when perfused over Fura-2-dextran injected rat hepatocytes. An antibody to **IPG** suppressed the inhibitory effect of insulin on the [Ca2+]i oscillations. Measurement of the rate of quench of cytoplasmic Fura-2 by extracellular Mn2+ showed that Ca2+ entry occurred continuously in the unstimulated cell and was not affected by phenylephrine or vasopressin. **IPG**, specifically, almost completely abolished the Mn2+ quench rate. Elevated extracellular [Ca2+] reversed the inhibitory effect of **IPG** on [Ca2+]i oscillations. We conclude that **IPG** inhibits the hepatocyte Ca2+ oscillatory by reducing the continuous Ca2+ influx that is required to sustain oscillations in [Ca2+]i.

L40 ANSWER 34 OF 41 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96333396 MEDLINE
DOCUMENT NUMBER: 96333396 PubMed ID: 8757890
TITLE: Structural similarities among malaria toxins insulin second messengers, and bacterial endotoxin.
AUTHOR: Caro H N; Sheikh N A; Taverne J; Playfair J H; **Rademacher T W**
CORPORATE SOURCE: Molecular Medicine Unit, Department of Molecular Pathology, University College London Medical School, United Kingdom.
SOURCE: INFECTION AND IMMUNITY, (1996 Aug) 64 (8) 3438-41. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19970203
Entered Medline: 19960926

AB Malaria toxin causes hypoglycemia and induction of tumor necrosis factor. Extracts of parasitized erythrocytes which were coeluted and copurified with one of the two subtypes of mammalian insulin-mimetic **inositolphosphoglycans** similarly induced fibroblast proliferation in the absence of serum. In addition, induction of tumor necrosis factor in macrophages by malaria toxin and by lipopolysaccharide from Escherichia coli was enhanced by pretreatment of these toxins with alpha-galactosidase. Thus, parasitized erythrocytes contain both soluble **inositolphosphoglycan**-like insulin second messengers and endotoxin-like lipidic molecules.

L40 ANSWER 35 OF 41 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 1996:747263 HCAPLUS
DOCUMENT NUMBER: 126:70435
TITLE: No change in insulin mediators in human skeletal muscle during isometric contraction or recovery
AUTHOR(S): Katz, A.; Hultman, E.; Huang, Laura; Villar-Palasi, C.; Larner, J.
CORPORATE SOURCE: Dep. Surgical Scis., Karolinska Hosp., Stockholm, Swed.
SOURCE: Hormone and Metabolic Research (1996), 28(10), 545-548

Search completed by David Schreiber 308-4292

CODEN: HMMRA2; ISSN: 0018-5043
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The rapid activation of glycogen synthase in human skeletal muscle during recovery from isometric contraction is dependent on an intact circulation, which suggests the requirement of an activating humoral factor. To det. whether the activating factor is insulin, muscle biopsies were obtained from subjects at rest, at fatigue, 3 min postexercise with an intact circulation, and 3 min postexercise during which circulation to the muscle was occluded. Two **inositol phosphoglycan** mediators of insulin action were isolated from the biopsies, and bioactivity was measured by detg. the effects of the isolated mediators on the activities of purified cAMP-dependent protein kinase, pyruvate dehydrogenase phosphatase and glycogen synthase phosphatase in vitro. Bioactivity was not altered by any condition compared with rest. These data suggest that changes in **inositol phosphoglycans** are not responsible for the circulation-dependent activation of glycogen synthase during recovery from exercise.

L40 ANSWER 36 OF 41 MEDLINE
ACCESSION NUMBER: 97030490 MEDLINE
DOCUMENT NUMBER: 97030490 PubMed ID: 8876431
TITLE: Characterization of a nucleotide stimulated aspartic proteinase in rat liver plasma membranes.
AUTHOR: Paule C R; Larner J
CORPORATE SOURCE: Department of Pharmacology, University of Virginia Medical School, Charlottesville 22908, USA.
CONTRACT NUMBER: AM 14334 (NIADDK)
SOURCE: JOURNAL OF BASIC AND CLINICAL PHYSIOLOGY AND PHARMACOLOGY, (1996) 7 (2) 121-36.
Journal code: 9101750. ISSN: 0792-6855.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19970115

AB **Inositol phosphoglycan** molecules are believed to mediate multiple intracellular actions of insulin. They are released from plasma membranes in response to insulin binding and are transported into the cell. Release of insulin mediators is stimulated by MnATP and MgATP and is inhibited by p-aminobenzamidine. **Inositol phosphoglycan** mediators may be released by a poorly characterized mechanism requiring proteolytic cleavage of an attached protein from the mediator and phospholipase cleavage of the mediator from its membrane anchor. We examined rat liver plasma membranes for proteinase activity stimulated by insulin and MnATP. Although we could not demonstrate insulin stimulation, we have found and characterized a nucleotide-stimulated aspartic proteinase bound to rat liver plasma membranes. We also detected and separated a soluble activating factor for the proteinase. The activating factor appears to be a protein with M(r) approximately 70 kDa.

L40 ANSWER 37 OF 41 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 94362552 MEDLINE
DOCUMENT NUMBER: 94362552 PubMed ID: 8081246
TITLE: **Inositolphosphoglycan** second messengers.

AUTHOR: **Rademacher T W**; Caro H; Kunjara S; Wang D Y; Greenbaum A L; **McLean P**
CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, United Kingdom.
SOURCE: BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH, (1994 Feb) 27 (2) 327-41.
Journal code: 8112917. ISSN: 0100-879X.
PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 20000303
Entered Medline: 19941013

AB The mechanisms by which cellular receptors can elicit different biological responses in a maturation state-dependent manner is one of the central problems in cell differentiation which remains to be resolved. The signals generated are likely to be due to additional (as yet unknown) transmembrane signalling pathways. In addition, the recent observation that a single growth factor receptor can activate a whole family of different putative second messengers and that the combinatorial interactions and stoichiometric ratios between the different messengers determine the resulting biological activities has opened up a whole new area of cell biology. It has been proposed that membrane GPI-anchors may function in signal transduction. We have recently confirmed the presence of a family of **inositolphosphoglycan** second messengers. Partial structural data suggests that these second messengers are not derived from known GPI membrane anchors and may thus constitute a novel class of non-protein-conjugated GPI.

L40 ANSWER 38 OF 41 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 92049385 MEDLINE
DOCUMENT NUMBER: 92049385 PubMed ID: 1719385
TITLE: Insulin-like effects of **inositol** phosphate-**glycan** on messenger RNA expression in rat hepatocytes.
AUTHOR: Alvarez L; Avila M A; Mato J M; Castano J G; Varela-Nieto I
CORPORATE SOURCE: Instituto de Investigaciones Biomedicas del Consejo Superior de Investigaciones Cientificas, Facultad de Medicina, Universidad Autonoma de Madrid, Spain.
SOURCE: MOLECULAR ENDOCRINOLOGY, (1991 Aug) 5 (8) 1062-8.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19980206
Entered Medline: 19911210

AB The ability of an **inositol** phosphate-**glycan** (**IPG**) to mimic the effects of insulin on regulation of the expression of specific mRNAs was studied in isolated hepatocytes from normal and diabetic rats. Incubation of normal liver cells with **IPG** (10 microM) during 90 min produced a 5-fold decrease in phosphoenolpyruvate carboxykinase (PEPCK) mRNA levels, which had been previously increased about 10-fold by incubation with 8-bromo-cAMP (0.1 mM). The effect of **IPG** was dose dependent and could not be

reproduced by galactose, glucosamine, or myo-**inositol**. **IPG** reduction of PEPCK mRNA is primarily due to a decrease in the rate of transcription of the gene, as judged by nuclear run-on transcription experiments performed in rat hepatoma H4IIE cells. In hepatocytes isolated from diabetic rats, treatment with 5 microM **IPG** for 15 min caused a 4-fold induction in the expression of alpha 2-microglobulin mRNA concomitantly with a 2.5-fold decrease in the level of PEPCK mRNA. Cleavage of **IPG** with nitrous acid abolished both the increase and the decrease in specific mRNAs levels. Glycosyl-phosphatidylinositol, the lipid **precursor** of **IPG**, did not modify either PEPCK or alpha 2-microglobulin mRNA levels. These data indicate that both positive and negative effects of insulin on the regulation of gene expression are mimicked by **IPG**
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L40 ANSWER 39 OF 41 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 90202781 MEDLINE
DOCUMENT NUMBER: 90202781 PubMed ID: 2156818
TITLE: 3H]myoinositol incorporation into phospholipids in liver microsomes from humans with and without type II diabetes. The lack of synthesis of glycosylphosphatidylinositol, precursor of the insulin mediator **inositol** phosphate **glycan**.
AUTHOR: Thakkar J K; Raju M S; Kennington A S; Foil B; Caro J F
CORPORATE SOURCE: Department of Medicine, School of Medicine, East Carolina University, Greenville, North Carolina 27858-4354.
CONTRACT NUMBER: PO1 DK-36296 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1990 Apr 5) 265 (10) 5475-81.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19970203
Entered Medline: 19900503

AB A class of **inositol** phosphate-containing oligosaccharides (**IPG**) derived from a membrane **glycan**-phosphatidylinositol precursor (GPI) has been identified as a possible mediator of insulin action. Saltiel's laboratory has recently communicated an in vitro assay for the synthesis of GPI in rat liver microsomes. Herein we have established this method in rat and human liver microsomes, it being our end point to evaluate if the pool of GPI was normal in diabetes and if failure of insulin to generate **IPG** from GPI could be involved in the mechanism of insulin resistance in Type II diabetes. However, subsequent to the detailed study of [3H]myoinositol incorporation into phospholipids in liver microsomes from our study subjects, we demonstrated by gas chromatography/mass spectrometry analysis that the material reported to be GPI is a mixture of lysophospholipids that does not contain hexosamine, ethanolamine, or amino acids.

L40 ANSWER 40 OF 41 MEDLINE
ACCESSION NUMBER: 91173542 MEDLINE
DOCUMENT NUMBER: 91173542 PubMed ID: 2077700
TITLE: The early development and evolution of the human brain.
AUTHOR: Crawford M A
CORPORATE SOURCE: Nuffield Laboratory of Comperative Medicine, Institute of

Young 09/719,909

Zoology, London, UK.
SOURCE: UPSALA JOURNAL OF MEDICAL SCIENCES. SUPPLEMENT, (1990) 48 43-78. Ref: 57
Journal code: 0331622. ISSN: 0300-9726.
Report No.: NASA-91173542.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19910512
Last Updated on STN: 19910512
Entered Medline: 19910422

AB THE CHEMISTRY OF THE BRAIN: The brain and nervous system is characterised by a heavy investment in lipid chemistry which accounts for up to 60% of its structural material. In the different mammalian species so far studied, only the 20 and 22 carbon chain length polyenoic fatty acids were present and the balance of the n-3 to n-6 fatty acids was consistently 1:1. The difference observed between species, was not in the chemistry but in the extent to which the brain is developed. This paper discusses the possibility that essential fatty acids may have played a part in it evolution. THE ORIGIN OF AIR BREATHING ANIMALS: The first phase of the planet's existence indulged in high temperature reactions in which oxygen combined with everything feasible: from silicon to make rocks to hydrogen to make water. Once the planet's temperature dropped to a point at which water could condense on the surface allowing chemical reactions to take place in it. The atmosphere was at that time devoid of oxygen so life evolved in a reducing atmosphere. Oxygen was liberated by photolysis of water and as a by-product of the blue-green algae through photosynthesis. When the point was reached at which oxidative metabolism became thermodynamically possible, animal life evolved with all the principle phyla establishing themselves within a relatively short space of geological time. (Bernal 1973). DHA and nerve cell membranes DHA AND NERVE CELL MEMBRANES: From the chemistry of contemporary algae it is likely that animal life evolved in an n-3 rich environment although not exclusively so as smaller amounts of n-6 fatty acids would have been present. A key feature of the first animals was the evolution of the photoreceptor: in examples of marine, amphibian and modern mammalian species, it has been found to use docosahexaenoic acid (DHA) as the principle membrane fatty acid in the phosphoglycerides. It is likely that the first animals did so as well. Coincidentally, the synaptic membranes involved in signal transduction also use high proportions of n-3 fatty acids. However, the n-6 fatty acids also find a place, in the **inositol** phosphoglyceride (**IPG**) which appears to be involved with **calcium** ion transport and hence signal activation and reception. Even in the photoreceptor, the **IPG** is an arachidonic acid rich phosphoglyceride. THE EVOLUTION OF MAMMALS AND THE LARGE BRAIN: The dominance of n-3 fatty acids in the food chain, persisted until the end of the Cretaceous period when the flowering plants followed on the disappearance of the giant cycads and ferns. A new set of species, the mammals, then evolved with a requirement for n-6 fatty acids for reproduction. This dependance was coincident with the flowering plants which for the first time produced protected seeds: these introduced a rich source of n-6 fatty acids. The brain size of the mammals tended to be relatively larger (that is in relation to body size) by comparison with the previous reptilian or egg laying systems. This process led to the large human brain. A crucial difference between man and other animals, is

undoubtedly the extent to which the brain and its peripheral attributes have been developed. This paper will address the possibility that the potential for the evolution of the large human brain may have been released by the evolving human primate occupying an ecological niche which offered a rich source of those nutrients specifically required for the brain. That niche is at the land/water interface.

L40 ANSWER 41 OF 41 MEDLINE
ACCESSION NUMBER: 89005725 MEDLINE
DOCUMENT NUMBER: 89005725 PubMed ID: 2844608
TITLE: Insulin-induced decrease in 5'-nucleotidase activity in skeletal muscle membranes.
AUTHOR: Klip A; Ramlal T; Douen A G; Burdett E; Young D; Cartee G D; Holloszy J O
CORPORATE SOURCE: Department of Cell Biology, Hospital for Sick Children, Toronto, Canada.
CONTRACT NUMBER: AG00078 (NIA)
DK 18986 (NIDDK)
SOURCE: FEBS LETTERS, (1988 Oct 10) 238 (2) 419-23.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198811
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881114

AB Insulin releases **inositol phosphoglycans** from myocytes in culture [(1986) Science 233, 967-972], which display insulinomimetic activity. Because 5'-nucleotidase is anchored to the membrane through inositol-containing phospholipid glycans, we investigated whether insulin could release the enzyme from the membrane. Membranes prepared from hindquarter muscles of rats perfused with insulin showed a 23% decrease in 5'-nucleotidase activity. Isolated membranes from muscle exposed to insulin in vitro also showed a small but reproducible decrease (9%) in 5'-nucleotidase activity relative to unexposed controls. Phospholipase C from Staphylococcus aureus released 60% of the membrane-bound 5'-nucleotidase. We propose that insulin may activate an endogenous phospholipase C that cleaves phospholipid-glycan-anchored proteins.